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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,687	11/21/2001	Luisa Iruela-Arispe	PF453P3	9708

22195 7590 06/04/2007

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
06/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/989,687	IRUELA-ARISPE ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-3,5-7 and 9-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3,5-7 and 9-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/8/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim 1 has been amended. Claims 1-3, 5-7, 9-32 are pending and under consideration.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, 7, and 9-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating an individual having a disease wherein angiogenesis or neovascularization contributes to the pathological state, comprising the administration of the instant METH polypeptides, does not reasonably provide enablement for a. method for treating an individual having a disease wherein angiogenesis or neovascularization contributes to counteract a pathological state, comprising the administration of the instant METH polypeptides The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The instant claims require the inhibition of angiogenesis by administration of the METH polypeptides recited in the claims and the treatment of diseases such as "vasculogenesis" granulations, hypertrophic scars, non-union fractures, scleroderma, myocardial angiogenesis, coronary angiogenesis, plaque neovascularization, wound granulation and atherosclerosis.

The art recognizes that myocardial angiogenesis, coronary angiogenesis, cerebral collaterals, ischemic limb angiogenesis are a result of hypoxic conditions within the tissue or organ and are a physiological response to maintain tissue viability (Ungar et al, Am J

Physiology, 1991, Vol. H1625-H1634, page H1625, first column, lines 15-17 under the abstract; Norrby et al, Int J Exp Path, 1992, Vol. 73, pp. 147-155, last sentence of abstract). Because the art teaches that these conditions are necessary to maintain oxygenated tissues in an injured organisms, it is unclear how an inhibitor of angiogenesis would be used in the treatment of such diseases. Notably, Fraser and Lunn (British Medical Bulletin, 2000, vol. 56, pp. 787-797) teach that stimulation of angiogenesis is desirable in patients with limb ischemia and myocardial ischemia (page 793, last four lines). The art also recognizes that the inhibition of angiogenesis in granulations slows down the healing of the wound (Hase et al, Digestion, 1989, Vol. 42, pp. 135-142, last sentence of abstract; Tsuchida et al, Digestion, 1990, Vol. 47, pp. 8-14). Here again, based on the teachings of the art as angiogenesis being a positive factor in the healing of wound granulations, one of skill in the art would be subject to undue experimentation without undue expectation of success in order to treat wound granulations with the instant METH polypeptides. Regarding the treatment of atherosclerosis and plaque neovascularizations, the art teaches a correlation with impaired endothelial cell growth manifest by adaptive growth responses of arteries and microvessels (abstract, last line). Thus, the angiogenic response to the endothelial growth defect appears to be an effect, rather than a cause of the atherosclerosis. There is no objective evidence in the specification that reversal of the angiogenesis would restore normal endothelial cell growth. Further, "non-union fractures" would benefit from the stimulating effect of neovascularization .

The claims also broadly encompass the treatment of "vasculogenesis". Vasculogenesis is a physiological means for promoting tissue viability. For instance, Petzer et al (Journal of Orthopaedic Research, 2007, Vol. 25, pp. 370-377) teach that vascularization of bone allografts results in long term viability of the graft sufficient to maintain weight bearing function, remodeling and healing requirements (page 977, lines 2-6). There is no guidance in the specification for how to use the instant METH polypeptides in conjunction with a bone graft undergoing neoangiogenesis.

Given the lack of guidance in the specification regarding how to use an angiogenesis inhibitor to treat diseases wherein angiogenesis or neovascularization contributes to counteract a pathological state, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the broadly clamed invention.

Claims 2, 6 and 21-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims require the administration of the METH polypeptides to an individual for birth control. When given the broadest reasonable interpretation, "an individual" encompasses both male and female individuals". The specification provides no teaches of how the inhibition of angiogenesis in a male contributes to the lack of reproductive ability. Further, Fraser and Lunn (British Medical Bulletin, 2000, Vol. 56, pp. 737-797) teach that angiogenesis is regulated in the reproductive tract by at least 20 angiogenic growth factors and inhibitors (page 788, third paragraph under "Angiogenic control mechanisms"). Fraser and Lunn teach that the mechanisms involved in these complex processes are not well understood, and points to the lack of nexus between animal studies of luteal function and luteal function in humans (page 790, lines 12-19). Thus the art is not mature with respect to the inhibition of luteolysis and angiogenic factors, and animal studies cannot be relied upon to provide for the deficient of data because of the lack of nexus between patterns of luteal function in animals and humans. Given the unreliability of the art, the lack of reliance on animal studies for modeling birth control in humans and the lack of guidance in the specification, one of skill in the art would be subject to undue experimentation in order to practice the instant method of inhibiting angiogenesis as it applied to birth control.

All other rejections and objections as set forth or mainlined in the previous Office action are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
5/14/2007